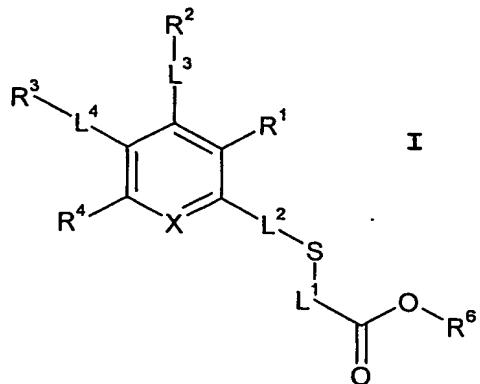


Claims

1. A compound of formula I:



wherein

5 X is N or CH;

R¹ is H, cyano, halo, hydroxy, hydroxamic acid, sulfhydryl or -NH₂; or C₁₋₄ alkyl optionally substituted by cyano, halo, hydroxy, hydroxamic acid, sulfhydryl or -NH₂; or -OR, -NHR, -NR₂ or -SR wherein R is C₁₋₄ alkyl optionally substituted by cyano, halo, hydroxy, hydroxamic acid, sulfhydryl or -NH₂;

10 R² is H, CF₃; or optionally substituted C₅₋₆ aryl, C₃₋₇ cycloalkyl, C₅₋₇ heterocyclyl or together with R³ an optionally substituted C₃₋₄ alkylene group wherein L³ and L⁴ are single bonds thus forming a C₅₋₆ ring fused with the aromatic ring to which L³ and L⁴ are attached;

15 R³ is H; or optionally substituted C₅₋₆ aryl, C₃₋₇ cycloalkyl, C₅₋₇ heterocyclyl or together with R² an optionally substituted C₃₋₄ alkylene group wherein L³ and L⁴ are single bonds thus forming a C₅₋₆ ring fused with the aromatic ring to which L³ and L⁴ are attached;

20 R⁴ is H; or optionally substituted C₅₋₆ aryl or C₅₋₇ heterocyclyl;

25 R⁶ is selected from H or optionally substituted C₁₋₇ alkyl, C₅₋₆ aryl and C₁₋₄ alkylene-C₅₋₆ aryl;

L¹ is optionally substituted C₁₋₄ alkylene, C₅₋₆ arylene,

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C_{1-4} alkylene- C_{5-6} arylene or $-L^5N(R^5)L^6-$, wherein L^5 and L^6 are independently selected from optionally substituted C_{1-4} alkylene and C_{5-6} arylene, and R^5 is H or C_{1-4} alkyl;

L^2 is a single bond; or optionally substituted C_{1-4}

5 alkylene or $-L^7C(=O)L^8-$, wherein L^7 and L^8 are independently selected from optionally substituted C_{1-4} alkylene and a single bond; and

10 L^3 and L^4 are independently selected from a single bond, optionally substituted C_{1-4} alkylene, $-L^9YN(OH)C(=O)L^{10}-$ and $-L^9C(=O)N(OH)YL^{10}-$, wherein L^9 and L^{10} are independently selected from optionally substituted C_{1-4} alkylene, C_{5-6} arylene, C_{1-4} alkylene- C_{5-6} arylene and a single bond, wherein Y is NH or a single bond;

15 or a pharmaceutically acceptable salt thereof for use in a method of therapy.

2. A compound according to claim 1 wherein R^1 is chosen from the group consisting of H and cyano.

20 3. A compound according to any one of the preceding claims wherein R^6 is H or C_{1-7} alkyl.

25 4. A compound according to any one of the preceding claims wherein L^1 is chosen from the group consisting of phenylene, $-CH(Ph)-$, $-CH_2$ -phenylene- and $-CH_2C(=O)NH$ -phenylene-.

30 5. A compound according to any one of the preceding claims wherein L^2 is a single bond or $-C(=O)CH_2-$.

6. A compound according to any one of the preceding claims wherein L^3 is chosen from the group consisting of a single bond, $-L^9YN(OH)C(=O)L^{10}-$ and $-L^9C(=O)N(OH)YL^{10}-$,

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wherein L^9 and L^{10} are independently selected from optionally substituted C_{1-4} alkylene, C_{5-6} arylene, C_{1-4} alkylene- C_{5-6} arylene and a single bond, and wherein Y is NH or a single bond.

5

7. A compound according to claim 6 wherein L^3 is a single bond.

8. A compound according to any one of the preceding 10 claims wherein L^4 is chosen from the group consisting of a single bond, $-L^9YN(OH)C(=O)L^{10}-$ and $-L^9C(=O)N(OH)YL^{10}-$, wherein L^9 and L^{10} are independently selected from optionally substituted C_{1-4} alkylene, C_{5-6} arylene, C_{1-4} alkylene- C_{5-6} arylene and a single bond, and wherein Y is NH or a single 15 bond.

9. A compound according to claim 8 wherein L^4 is selected from the group consisting of $-CH_2N(OH)C(=O)-$, 20 $-phenylene-CH_2N(OH)C(=O)-$, $-phenylene-NHN(OH)C(=O)-$ and $-CH_2C(=O)N(OH)-$.

10. A compound according to any one of the preceding claims wherein X is CH.

25 11. A compound according to claim 10 wherein one of R^1 , R^2 and R^4 are H.

12. A compound according to claim 10 wherein two of R^1 , 30 R^2 and R^4 are H.

13. A compound according to claim 10 wherein R^1 , R^2 and R^4 are all H.

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14. A compound according to claim 10 wherein one of R^2 and R^3 is optionally substituted C_{5-6} aryl, C_{3-7} cycloalkyl or C_{5-7} heterocyclyl.

5 15. A compound according to claim 14 wherein R^3 is optionally substituted C_{5-6} aryl, C_{3-7} cycloalkyl or C_{5-7} heterocyclyl.

10 16. A compound according to claim 14 wherein R^3 is optionally substituted phenyl or C_{3-7} cycloalkyl.

17. A compound according to claim 14 wherein R^3 is phenyl or cyclopentyl.

15 18. A compound according to claim 10 wherein L^1 is phenylene or $-CH(Ph)-$.

19. A compound according to claim 10 wherein one of L^3 and L^4 is a single bond.

20 20. A compound according to claim 19 wherein L^3 is a single bond.

21. A compound according to any one of claims 1 to 9
25 wherein X is N.

22. A compound according to claim 21 wherein R^1 is cyano or hydroxamic acid.

30 23. A compound according to claim 21 wherein R^2 is selected from the group consisting of optionally substituted C_{5-6} aryl, C_{5-7} heterocyclyl, CF_3 and, together with R^3 , an optionally substituted butylene group wherein L^3 and L^4 are

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single bonds thus forming a C₆ ring fused with the aromatic ring to which L³ and L⁴ are attached.

24. A compound according to claim 23 wherein R² is
5 selected from optionally substituted C₅₋₆ aryl or C₅₋₇ heterocyclyl.

25. A compound according to claim 23 wherein R² is selected from optionally substituted phenyl or thiophenyl.

10

26. A compound according to claim 23 wherein R² is selected from the group consisting of thiophenyl, phenyl, p-chlorophenyl, p-methoxyphenyl, o-methoxyphenyl and p-fluorophenyl.

15

27. A compound according to any one of claims 23 to 25 wherein R² is a monosubstituted phenyl group with the substituent group being in the para position.

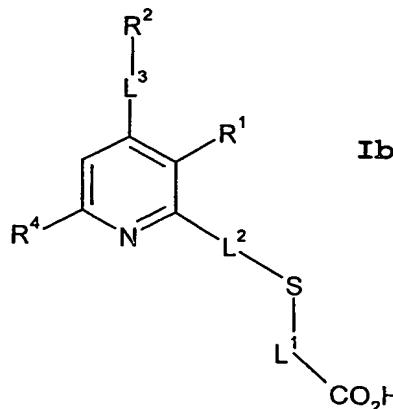
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28. A compound according to any one of claims 21 to 27 wherein R³ is H or, together with R², an optionally substituted butylene group wherein L³ and L⁴ are single bonds thus forming a C₆ ring fused with the aromatic ring to which L³ and L⁴ are attached.

25

29. A compound according to claim 28 wherein R³ is H and L⁴ is a single bond such that the compound is of formula Ib:

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30. A pharmaceutical composition comprising a compound according to any one of the preceding claims or a

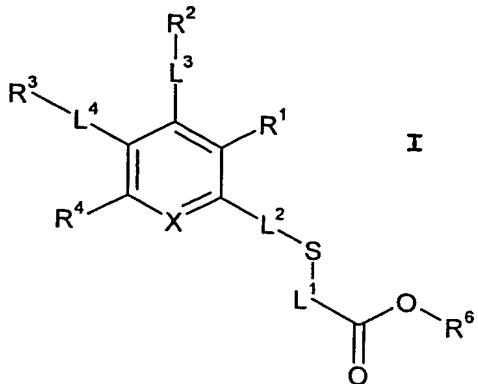
5 pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable carrier or diluent.

31. Use of a compound according to any one of claims 1 to 29 or a pharmaceutically acceptable salt thereof in the preparation of a medicament for the treatment of a condition alleviated by inhibition of glyoxalase I.

32. A method of treating a condition which can be alleviated by inhibition of glyoxalase I, which method comprises administering to a patient in need of treatment an effective amount of a compound according to any one of claims 1 to 29, or a pharmaceutically acceptable salt thereof.

20 33. A compound of formula **I**:

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or a salt, solvate or chemically protected form thereof
wherein

X is N or CH;

5 R¹ is H, cyano, halo, hydroxy, hydroxamic acid, sulfhydryl or -NH₂; or C₁₋₄ alkyl optionally substituted by cyano, halo, hydroxy, hydroxamic acid, sulfhydryl or -NH₂; or -OR, -NHR, -NR₂ or -SR wherein R is C₁₋₄ alkyl optionally substituted by cyano, halo, hydroxy, hydroxamic acid, sulfhydryl or -NH₂;

10 R² is H, CF₃; or optionally substituted C₅₋₆ aryl, C₃₋₇ cycloalkyl, C₅₋₇ heterocyclyl or together with R³ an optionally substituted C₃₋₄ alkylene group wherein L³ and L⁴ are single bonds thus forming a C₅₋₆ ring fused with the aromatic ring to which L³ and L⁴ are attached;

15 R³ is H; or optionally substituted C₅₋₆ aryl, C₃₋₇ cycloalkyl, C₅₋₇ heterocyclyl or together with R² an optionally substituted C₃₋₄ alkylene group wherein L³ and L⁴ are single bonds thus forming a C₅₋₆ ring fused with the aromatic ring to which L³ and L⁴ are attached;

20 R⁴ is H; or optionally substituted C₅₋₆ aryl or C₅₋₇ heterocyclyl;

R⁶ is selected from H or optionally substituted C₁₋₇ alkyl, C₅₋₆ aryl and C₁₋₄ alkylene-C₅₋₆ aryl;

25 L¹ is optionally substituted C₁₋₄ alkylene, C₅₋₆ arylene, C₁₋₄ alkylene-C₅₋₆ arylene or -L⁵N(R⁵)L⁶-, wherein L⁵ and L⁶

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are independently selected from optionally substituted C_{1-4} alkylene and C_{5-6} arylene, and R^5 is H or C_{1-4} alkyl;

5 L^2 is a single bond; or optionally substituted C_{1-4} alkylene or $-L^7C(=O)L^8-$, wherein L^7 and L^8 are independently selected from optionally substituted C_{1-4} alkylene and a single bond; and

10 L^3 and L^4 are independently selected from a single bond, optionally substituted C_{1-4} alkylene, $-L^9YN(OH)C(=O)L^{10}-$ and $-L^9C(=O)N(OH)YL^{10}-$, wherein L^9 and L^{10} are independently selected from optionally substituted C_{1-4} alkylene, C_{5-6} arylene, C_{1-4} alkylene- C_{5-6} arylene and a single bond, wherein Y is NH or a single bond; and wherein the compound contains at least one $-C(=O)N(OH)-$ group.

15

34. A compound according to claim 33 wherein at least one of R^1 , L^3 or L^4 comprises a $-C(=O)N(OH)-$ group.

20 35. A compound according to claim 33 wherein L^4 comprises a $-C(=O)N(OH)-$ group.

36. A compound according to any one of claims 33 to 35 wherein L^4 is a $L^9-C(=O)N(OH)-$ group.

25 37. A compound according to claim 36 wherein L^9 is selected from C_{1-4} alkylene and C_{5-6} arylene.

30 38. A compound according to claim 36 wherein L^9 is methylene or phenylene.

39. A compound according to any one of claims 33 to 38 wherein X is CH.

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40. A compound according to any one of claims 33 to 39 wherein at least one of R¹, R² and R⁴ is H.

5 41. A compound according to any one of claims 33 to 39 wherein at least two of R¹, R² and R⁴ are H.

42. A compound according to any one of claims 33 to 39 wherein all of R¹, R² and R⁴ are H.

10 43. A compound according to any one of claims 33 to 42 wherein R³ is optionally substituted C₅₋₆ aryl.

15 44. A compound according to claim 43 wherein R³ is phenyl.

45. A compound according to any one of claims 33 to 44 wherein R⁶ is H or C₁₋₇ alkyl.

20 46. A compound according to claim 45 wherein R⁶ is H or C₁₋₃ alkyl.

25 47. A compound according to any one of claims 33 to 46 wherein L¹ is phenylene, -CH(Ph)-, -CH₂-phenylene- or -CH₂C(=O)NH-phenylene-.

48. A compound according to any one of claims 33 to 47 wherein L² is a single bond or -C(=O)CH₂-.

30 49. A compound according to any one of claims 33 to 48 wherein L³ is a single bond.